

WHAT IS CLAIMED IS:

1. A liquid composition for the delivery of biologically active substances, comprising:
a non-water soluble, high viscosity, liquid carrier material comprising a nonpolymeric ester or mixed ester of one or more carboxylic acids, having a viscosity of at least 5,000 cP at 37 C, that does not crystallize neat under ambient or physiological conditions.
2. The composition of claim 1, wherein at least one of said one or more carboxylic acids is a hydroxy acid.
3. The composition of claim 1, wherein said nonpolymeric ester or mixed ester is obtained by a ring opening reaction of a lactone or a cyclic carbonate.
4. The composition of claim 2, wherein said nonpolymeric ester or mixed ester comprises 2 to about 20 hydroxy acid moieties.
5. The composition of claim 3, wherein said nonpolymeric ester or mixed ester comprises 2 to about 20 hydroxy acid moieties.
6. The composition of claim 1, wherein said nonpolymeric ester or mixed ester of one or more carboxylic acids comprises a polyoxy alcohol moiety having from 2 to about 20 hydroxy moieties.

7. The composition of claim 1, wherein said nonpolymeric ester or mixed ester comprises an alcohol moiety having one or more terminal hydroxy moieties esterified with a carboxylic acid obtained by alcoholysis of a carboxylic acid anhydride.
8. The composition of claim 7, wherein said carboxylic acid anhydride is a cyclic anhydride.
9. The composition of claim 1, wherein said nonpolymeric ester or mixed ester comprises an alcohol moiety having one or more terminal hydroxy moieties esterified with an amino acid.
10. The composition of claim 6, wherein the nonpolymeric ester or mixed ester comprises an alcohol moiety obtained by removing one or more hydrogen atoms from a alcohol selected from the group consisting of: monofunctional C₁-C₂₀ alcohols, difunctional C₁-C₂₀ alcohols, trifunctional alcohols, hydroxy-containing carboxylic acids, hydroxy-containing amino acids, phosphate- containing alcohols, tetrafunctional alcohols, sugar alcohols, monosaccharides, and disaccharides, sugar acids, and polyether polyols.
11. The composition of claim 10, wherein the monofunctional C₁-C₂₀ alcohol is dodecanol.
12. The composition of claim 10, wherein the difunctional C₁-C₂₀ alcohol is a hexanediol.
13. The composition of claim 10, wherein the trifunctional alcohol is glycerol.

14. The composition of claim 10, wherein the hydroxy-containing carboxylic acid is glycolic acid or lactic acid or a combination thereof.
15. The composition of claim 10, wherein the hydroxy-containing amino acid is serine.
16. The composition of claim 10, wherein the hydroxy-containing acid is hydroxybutyric acid, hydroxyvaleric acid, hydroxycaproic acid, or a mixture of one or more of these.
17. The composition of claim 10, wherein the phosphate containing alcohol is ATP.
18. The composition of claim 10, wherein the tetrafunctional alcohol is pentaerythritol.
19. The composition of claim 10, wherein the sugar alcohol is mannitol or sorbitol.
20. The composition of claim 10, wherein the monosaccharide is glucose or fructose.
21. The composition of claim 10, wherein the disaccharide is sucrose.
22. The composition of claim 10, wherein the sugar acid is glucuronic acid.
23. The composition of claim 10, wherein the polyether polyol is a polyglycerol ether containing from 1 to about 10 glycerol units or a polyethyleneglycol containing 1 to about 20 ethylene glycol units.

24. The composition of claim 3, wherein the lactone is selected from the group consisting of glycolide, lactide, ϵ -caprolactone, butyrolactone, valerolactone, and wherein the cyclic carbonate is selected from the group consisting of trimethylene carbonate, propylene carbonate.

25. The composition of claim 1, further comprising a biologically active substance.

26. The composition of claim 25, wherein said biologically active substance is encapsulated within a microsphere.

27. The composition of claim 25, wherein the biologically active substance is selected from the group consisting of a protein, a peptide, a nucleoprotein, a mucoprotein, a lipoprotein, and a synthetic polypeptide.

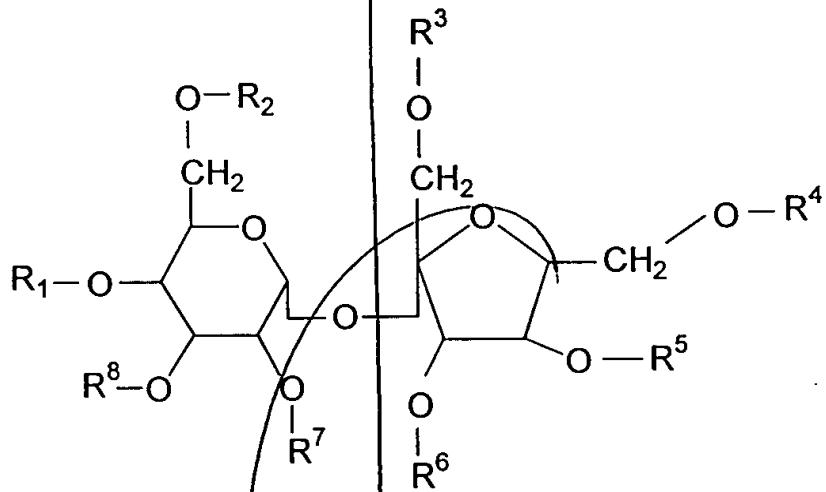
28. The composition of claim 27, wherein the protein is selected from group consisting of human growth hormone, fibroblast growth factor (FGF), erythropoietin (EPO), platelet derived growth factor (PDGF), granulocyte colony stimulating factor (g-CSF), bovine somatotropin (BST), tumor necrosis factor (TNF), transforming growth factor-beta (TGF-Beta), interleukins, insulin, and interferon.

29. The composition of claim 25, wherein the biologically active substance is selected from the group consisting of nucleic acid, nucleotides, nucleosides, oligonucleotides, and genes.

30. The composition of claim 29, wherein the nucleic acid comprises DNA, RNA, or a fragment thereof.

31. The liquid composition according to claim 1, wherein the high viscosity liquid carrier material has a structure selected from the group consisting of:

I:

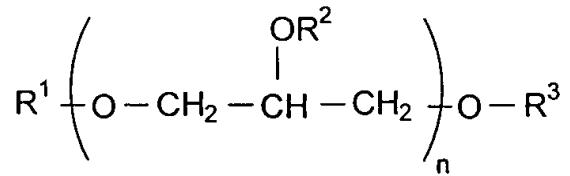


wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 are independently selected from the group consisting of hydrogen, alkanoyl, hydroxy-substituted alkanoyl, and acyloxy-substituted alkanoyl;

wherein at least three of R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 are other than hydrogen; and

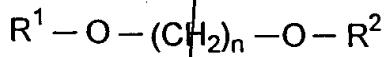
wherein when R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 are selected from the group consisting of acetyl and isobutyryl, at least three of R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , and R^8 are acetyl;

II:



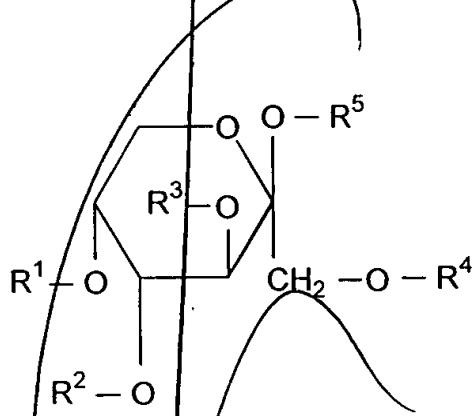
wherein R^1 , R^2 , and R^3 are independently selected from the group consisting of hydrogen, alkanoyl, hydroxy-substituted alkanoyl, and acyloxy-substituted alkanoyl and wherein n is between 1 and 20;

III:

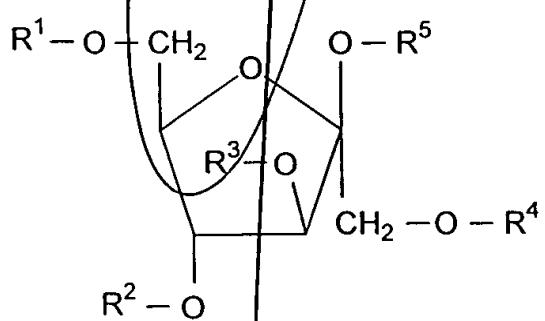


wherein n is an integer between 4 and 8, and R^1 and R^2 are independently selected from the group consisting of hydrogen, alkanoyl, hydroxy-substituted alkanoyl, and acyloxy-substituted alkanoyl;

IV:

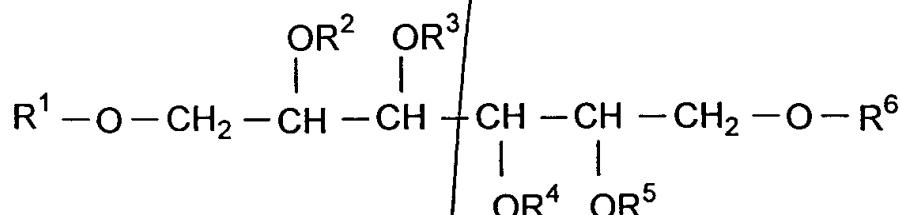


V:

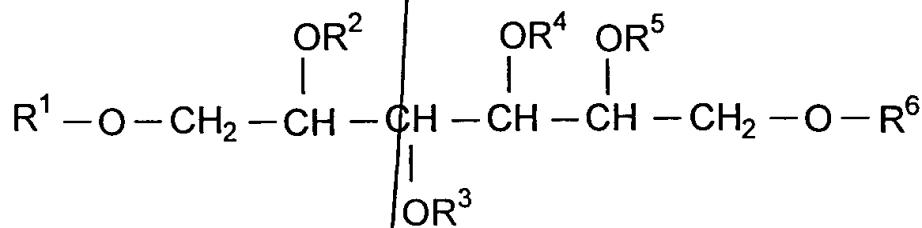


wherein R¹, R², R³, R⁴, and R⁵ are independently selected from the group consisting of hydrogen, alkanoyl, hydroxy-substituted alkanoyl, and acyloxy-substituted alkanoyl;

VI:

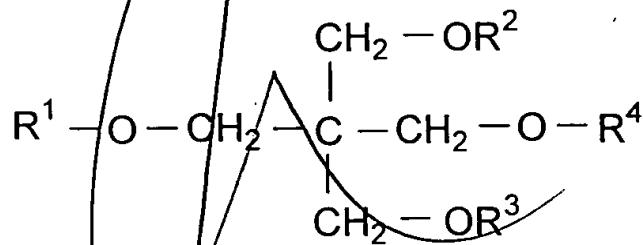


VII:



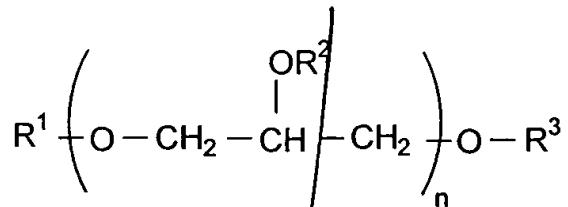
wherein R¹, R², R³, R⁴, R⁵, and R⁶ are independently selected from the group consisting of hydrogen, alkanoyl, hydroxy-substituted alkanoyl, and acyloxy-substituted alkanoyl;

VIII:

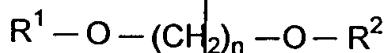


wherein R¹, R², R³, and R⁴ are independently selected from the group consisting of hydrogen, alkanoyl, hydroxy-substituted alkanoyl, and acyloxy-substituted alkanoyl.

32. The composition of claim 31, wherein the high viscosity liquid carrier comprises a structure selected from the group consisting of:

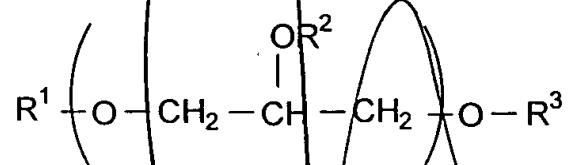


wherein n is 1 and R¹, R², and R³ are independently selected from the group consisting of hydrogen, alkanoyl, hydroxy-substituted alkanoyl, and acyloxy-substituted alkanoyl; and



wherein n is 6, and R¹ and R² are independently selected from the group consisting of hydrogen, alkanoyl, hydroxy-substituted alkanoyl, and acyloxy-substituted alkanoyl.

33. The composition according to claim 32, wherein the high viscosity liquid carrier comprises the structure:



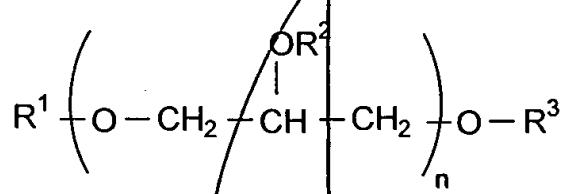
wherein n is 1 and at least one of R¹, R², and R³ are independently selected from the group consisting of hydroxy-substituted alkanoyl, and acyloxy-substituted alkanoyl.

34. The composition according to claim 33, wherein R¹, R², and R³ are independently selected from the group consisting of lactoyl, polylactoyl, ϵ -caproyl, hydroxyacetyl, and polyhydroxyacetyl.

35. The composition of claim 33, wherein R¹, R², and R³ are independently selected from the group consisting of polylactoyl and ϵ -caproyl.

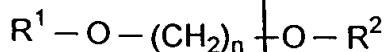
36. The composition of claim 33, wherein R¹, R², and R³ are independently selected from the group consisting of polylactoyl and polyhydroxyacetyl.

37. The composition of claim 32, wherein the high viscosity liquid carrier comprises the structure:



wherein n is 1 and at least one of R¹, R², and R³ are independently selected from the group consisting of alkanoyl, hydroxy-substituted alkanoyl, and acyloxy-substituted alkanoyl, each having from 2 to 4 carbon atoms.

38. The composition of claim 32, wherein the high viscosity liquid carrier comprises the structure:



wherein n is 6, and R¹ and R² are independently selected from the group consisting of lactoyl, polylactoyl, ε-caproyl, hydroxyacetyl, and polyhydroxyacetyl.

39. The composition of claim 38, wherein R¹ and R² are independently selected from the group consisting of polylactoyl and ε-caproyl

40. The composition of claim 38, wherein R¹ and R² are independently selected from the group consisting of polylactoyl and polyhydroxyacetyl.

41. The composition of claim 1, further comprising a solvent for the high viscosity liquid carrier material.

42. The composition of claim 41, wherein the solvent is selected from the group consisting of acetone, benzyl alcohol, benzyl benzoate, N-(betahydromethyl) lactamide, butylene glycol, caprolactam, caprolactone, corn oil, decylmethylsulfoxide, dimethyl ether, dimethyl sulfoxide, 1-dodecylazacycloheptan-2-one, ethanol, ethyl acetate, ethyl lactate, ethyl oleate, glycerol, glycofurool (tetraglycol), isopropyl myristate, methyl acetate, methyl ethyl ketone, N-methyl-2-pyrrolidone, esters of caprylic and/or capric acids with glycerol or alkylene glycols, oleic acid, peanut oil, polyethylene glycol, propylene carbonate, 2-pyrrolidone, sesame oil, [±]-2,2-dimethyl-1,3-dioxolane-4-methanol, tetrahydrofuran, diethylene glycol monoethyl ether, carbitol, triacetin, triethyl citrate, and combinations thereof.

43. The composition of claim 41, wherein the solvent is selected from the group consisting of trichlorofluoromethane, dichlorofluoromethane, tetrafluoroethane (R-134a), dimethyl ether, propane, butane, and combinations thereof.

44. The composition of claim 41, wherein the solvent is selected from the group consisting of benzyl benzoate, dimethyl sulfoxide, ethanol, ethyl lactate, glycerol, glycofurol (tetraglycol), *N*-methyl-2-pyrrolidone, caprylic/capric triglyceride, polyethylene glycol, propylene carbonate, 2-pyrrolidone, and combinations thereof.

45. The composition of claim 1, wherein the composition is encapsulated within a microsphere.

46. The composition of claim 1, wherein the composition further comprises a biologically active substance encapsulated within a microsphere.

47. The composition of claim 1, wherein the composition is in the form of an emulsion.

48. The composition of claim 1, further comprising an additive.

49. The composition of claim 48, wherein the additive is selected from the group consisting of biodegradable polymers, non-biodegradable polymers, natural oils, synthetic oils, carbohydrates, carbohydrate derivatives, inorganic salts, inert organic compounds, and water.

50. A method of administering a biologically active substance to a plant or animal in need thereof, comprising:

administering to the plant or animal a composition comprising:

a non-water soluble, high viscosity, liquid carrier material comprising a nonpolymeric ester or mixed ester of one or more carboxylic acids, having a viscosity of at least 5,000 cP at 37 °C, that does not crystallize neat under ambient or physiological conditions; and

a biologically active substance.

51. The method of claim 50, wherein the composition further comprises a solvent in which the non-water soluble, high viscosity, liquid carrier material is soluble.

52. The method of claim 51, further comprising allowing said solvent to diffuse or migrate away from said non-water soluble, high viscosity, liquid carrier material, thereby increasing the viscosity of the composition.

53. The method of claim 50, wherein said composition releases said biologically active material from the composition into the tissue of the plant or animal over time.

54. The method of claim 50, wherein said administering comprises administering by injection.

55. The method of claim 50, wherein said administering comprises administering rectally.

56. The method of claim 50, wherein said administering comprises administering intravaginally.

57. The method of claim 50, wherein said administering comprises administering intranasally.

58. The method of claim 50, wherein said administering comprises administering topically.

59. The method of claim 50, wherein said administering comprises pulmonary administration.

60. A medical or surgical implant, film, or graft composition comprising:
a non-water soluble, high viscosity, liquid carrier material comprising a nonpolymeric ester or mixed ester of one or more carboxylic acids, having a viscosity of at least 5,000 cP at 37 C, that does not crystallize near under ambient or physiological conditions.

61. The medical or surgical implant, film, or graft composition according to claim 60, wherein the non-polymeric, non-water soluble, high viscosity liquid carrier material has a viscosity of at least 10,000 cP at 37°C.

62. The medical or surgical implant, film, or graft composition according to claim 61, wherein the non-polymeric, non-water soluble, high viscosity liquid carrier material has a viscosity of at least 15,000 cP at 37°C.
63. The medical or surgical implant, film, or graft composition according to claim 62, wherein the non-polymeric, non-water soluble, high viscosity liquid carrier material has a viscosity of at least 20,000 cP at 37°C.
64. The medical or surgical implant, film, or graft composition according to claim 63, wherein the non-polymeric, non-water soluble, high viscosity liquid carrier material has a viscosity of at least 25,000 cP at 37°C.
65. The medical or surgical implant, film, or graft composition according to claim 64, wherein the non-polymeric, non-water soluble, high viscosity liquid carrier material has a viscosity of at least 50,000 cP at 37°C.
66. The medical or surgical implant, film, or graft composition according to claim 60, wherein the non-polymeric, non-water soluble, high viscosity liquid carrier material further comprises an additive.
67. The medical or surgical implant, film, or graft composition according to claim 66, wherein the additive is selected from the group consisting of water, biodegradable polymers or

oligomers, non-biodegradable polymers or oligomers, natural oils, synthetic oils, carbohydrates, carbohydrate derivatives, inorganic salts, and inert organic compounds.

68. The medical or surgical implant, film, or graft composition according to claim 60, further comprising a biologically active substance for controlled delivery.

69. The medical or surgical implant, film, or graft composition according to claim 60, which is a block for surgical adhesions.

70. The medical or surgical implant, film, or graft composition according to claim 60, which is a void filler in biological tissue.

71. The medical or surgical implant, film, or graft composition according to claim 60, which is a guide for tissue regeneration.

72. The medical or surgical implant, film, or graft composition according to claim 60, which is a hemostat.

73. The medical or surgical implant, film, or graft composition according to claim 60, which is a tissue adhesive.

74. The medical or surgical implant, film, or graft composition according to claim 60, which is a biological tissue scaffold.

75. The medical or surgical implant, film, or graft composition according to claim 60, which is a wound dressing.

76. The medical or surgical implant, film, or graft composition according to claim 60, wherein the non-polymeric non-water soluble liquid carrier material is present in an amount from about 99.5 percent to about 10 percent by weight, relative to the total weight of the composition.

77. The medical or surgical implant, film, or graft composition according to claim 60, wherein the non-polymeric non-water soluble liquid carrier material is present in an amount from about 99.5 percent to about 25 percent by weight, relative to the total weight of the composition.

78. A medical or surgical implantable or sprayable composition comprising a mixture of:

- (a) a non-polymeric, non-water soluble, high viscosity liquid carrier material having a viscosity of at least 5000 cP at 37 °C that does not crystallize neat under ambient or physiological conditions; and
- (b) a solvent in which the non-polymeric, non-water soluble liquid carrier material is soluble;

wherein the mixture has a viscosity of less than approximately 6,000 cP at 37 °C.

79. The medical or surgical implantable or sprayable composition according to claim 78, wherein the solvent is selected from the group consisting of ethanol, dimethylsulfoxide, ethyl

lactate, ethyl acetate, benzyl alcohol, triacetin, 2-pyrrolidone, *N*-methylpyrrolidone, propylene carbonate, glycofurol, and any aerosol propellant.

80. The medical or surgical implantable or sprayable composition according to claim 78, wherein the solvent in which the non-polymeric, non-water soluble liquid carrier material is soluble is present in an amount of from about 1% to about 90 % by weight, relative to the weight of the implantable or sprayable composition.

81. The medical or surgical implantable or sprayable composition according to claim 80, wherein the solvent in which the non-polymeric, non-water soluble liquid carrier material is soluble is present in an amount of from about 10% to about 90 % by weight, relative to the weight of the implantable or sprayable composition.

82. The medical or surgical implantable or sprayable composition according to claim 60, wherein the mixture has a viscosity of less than about 4,000 cP at 37 °C.

83. The medical or surgical implantable or sprayable composition according to claim 82, wherein the mixture has a viscosity of less than about 1,000 cP at 37 °C.

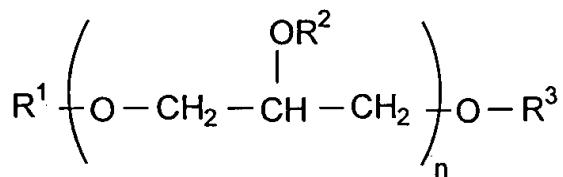
84. A method for the *in vivo* formation of an implant, film, or graft in a patient in need thereof, comprising:

- (1) contacting a mixture comprising:

- (a) a non-water soluble, high viscosity, liquid carrier material comprising a nonpolymeric ester or mixed ester of one or more carboxylic acids, having a viscosity of at least 5,000 cP at 37 °C, that does not crystallize neat under ambient or physiological conditions; and
- (b) a solvent in which the non-polymeric, non-water soluble liquid carrier material is soluble;
- wherein the mixture has a viscosity of less than approximately 6000 cP at 37 °C; with the tissue of the patient; and
- (2) allowing the solvent to dissipate or diffuse into the tissue of the patient, thereby forming an implant, film, or graft of the non-polymeric, non-water soluble, high viscosity liquid carrier material.
85. The method according to claim 84, wherein said contacting comprises coating a vascular graft with said mixture and implanting said vascular graft in the patient.
86. The method according to claim 84, wherein said contacting comprises injection or spraying of said mixture into or onto the tissue of the patient.
87. A method of administering a medical or surgical implant, film, or graft composition, comprising placing a non-water soluble, high viscosity, liquid carrier material comprising a nonpolymeric ester or mixed ester of one or more carboxylic acids, having a viscosity of at least 5,000 cP at 37 °C, that does not crystallize neat under ambient or physiological conditions into contact with the tissue of a patient in need thereof.

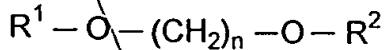
SVB 88. A compound having a structure selected from the group consisting of:

PY
II:



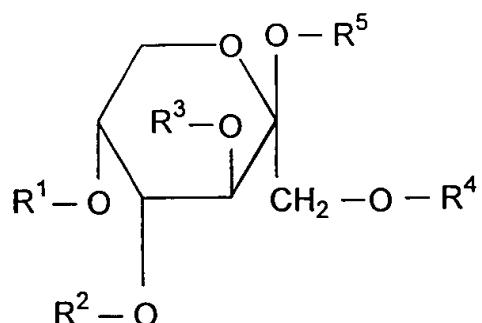
wherein R^1 , R^2 , and R^3 are independently selected from the group consisting of hydrogen, alkanoyl having 2 to 6 carbons, hydroxy-substituted alkanoyl having 2 to 6 carbons, and acyloxy-substituted alkanoyl having 2 to 6 carbons, wherein n is between 1 and 20, and wherein at least one of R^1 , R^2 , and R^3 is other than hydrogen;

III:

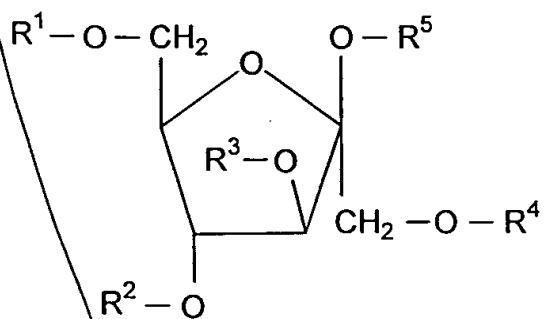


wherein n is an integer between 4 and 8, and R^1 and R^2 are independently selected from the group consisting of hydrogen, alkanoyl having 2 to 6 carbons, hydroxy-substituted alkanoyl having 2 to 6 carbons, and acyloxy-substituted alkanoyl having 2 to 6 carbons, and wherein at least one of R^1 and R^2 is other than hydrogen;

IV:

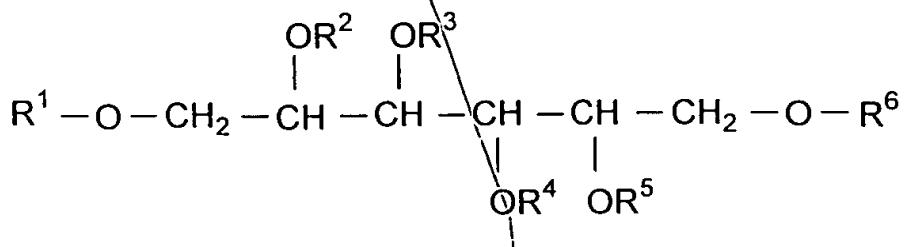


V:



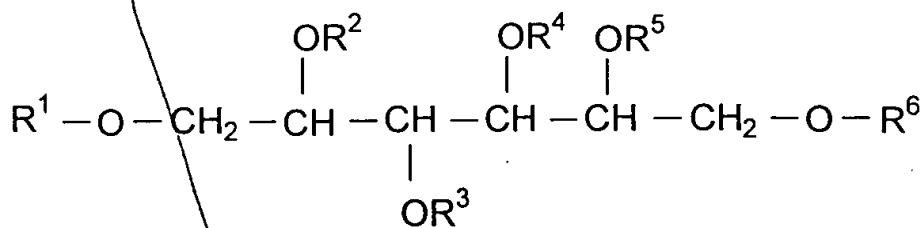
wherein R^1 , R^2 , R^3 , R^4 , and R^5 are independently selected from the group consisting of hydrogen, alkanoyl having 2 to 6 carbons, hydroxy-substituted alkanoyl having 2 to 6 carbons, and acyloxy-substituted alkanoyl having 2 to 6 carbons, and wherein at least one of R^1 , R^2 , R^3 , R^4 , and R^5 is other than hydrogen;

VI:



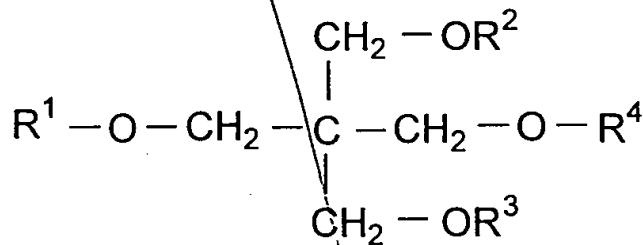
VII:

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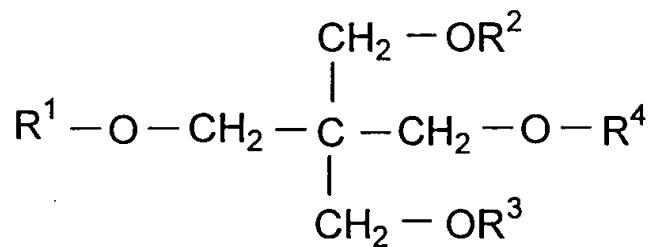
wherein R^1 , R^2 , R^3 , R^4 , R^5 , and R^6 are independently selected from the group consisting of hydrogen, alkanoyl having 2 to 6 carbons, hydroxy-substituted alkanoyl having 2 to 6 carbons, and acyloxy-substituted alkanoyl having 2 to 6 carbons, and wherein at least one of R^1 , R^2 , R^3 , R^4 , R^5 , and R^6 is other than hydrogen;

VIII:



wherein R^1 , R^2 , R^3 , and R^4 are independently selected from the group consisting of hydrogen, alkanoyl having 2 to 6 carbons, hydroxy-substituted alkanoyl having 2 to 6 carbons, and acyloxy-substituted alkanoyl having 2 to 6 carbons, and wherein at least one of R^1 , R^2 , R^3 , and R^4 is other than hydrogen.

89. The compound according to claim E, having the structure:



wherein R^1 , R^2 , R^3 , and R^4 are independently selected from the group consisting of hydrogen, alkanoyl having 2 to 6 carbons, hydroxy-substituted alkanoyl having 2 to 6 carbons, and acyloxy-substituted alkanoyl having 2 to 6 carbons, and wherein at least one of R^1 , R^2 , R^3 , and R^4 is other than hydrogen.

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